EXPANDED ABSTRACT

The essential role of luminal BK channels in distal colonic K^+ secretion

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Abstract : Distal colonic K^+ excretion is determined by the balance of K^+ absorption and K^+ secretion of the enterocytes. K^+ secretion occurs via active basolateral K^+ uptake mostly via the NKCC1 co-transporter followed by K^+ exit via a luminal K^+ channel. The specific focus here is directed towards the luminal secretory K^+ channel (1). Several recent observations highlight the pivotal role of the large conductance, Ca^{2+}-activated $K_{Ca}1.1$ (BK, KCNMA) channel as the only functionally relevant luminal K^+ efflux pathway in mouse distal colon (2, 3). This conclusion was based on defining results from BK knock-out mice. The following key observations were made : 1. BK channels mediate the resting distal colonic K^+ secretion (2, 4), 2. They are acutely stimulated by activation of luminal nucleotide receptor and elevations of intracellular Ca^{2+} (2, 4, 5), 3. Colonic BK channels are up-regulated by increases of plasma aldosterone (3), 4. In addition, the cAMP-stimulated distal colonic K^+ secretion is apparently mediated *via* BK channels, 5. Finally, aldosterone was found to up-regulate specifically the ZERO (*e.g.* cAMP activated) C-terminal splice variant of the BK channel. In summary, we suggest that the sole exit pathway for transcellular K^+ secretion in mammalian distal colon is the BK channel, which is the target for short term intracellular Ca^{2+} and cAMP activation and long term aldosterone regulation. J. Med. Invest. 56 Suppl. : 301, December, 2009

Keywords **:** *K^+ channel, ion secretion, colon, epithelium*

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